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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/088,090	06/21/2002	Stephen Arkinstall	220316USOPCT	7121

22850 7590 07/08/2003

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EXAMINER	
CHANG, CELIA C	
ART UNIT	**PAPER NUMBER**
1625	9

DATE MAILED: 07/08/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/088,090	Applicant(s) ARKINSTALL ET AL.	
	Examiner Celia Chang	Art Unit 1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *10 April 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1-28* is/are pending in the application.

4a) Of the above claim(s) *10-16* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1-9 and 17-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 7 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Applicant's election with traverse of Group I, claims 7-8, 24-25 with example 1 as the elected species in Paper No. 8, dated April 10, 2003 is acknowledged. The traversal is on the grounds that the office has not applied the same standard of unity of invention as the International Search authority and the Office has not shown that a burden exists in examining the entire application. This is not found persuasive because it was clearly delineated that under PCT Administrative Instruction Annex B, section (f) "Markush Practice" paragraph (f)(i)(B)(2)v, it was instructed that:

> "When dealing with alternatives, if it can be shown that at least one Markush alternative is ***not*** novel over the prior art, the question of unity of invention shall be reconsidered by the examiner"

Applicants' attention is particularly drawn to the enormous number of "X" references being cited in the International Search Report. Further, it was decided by the International Preliminary Examination Authority that claims 1-5, 13-16, 17-19 are ***not*** novel (see form 409). With clear record that the Markush claims do not belong to the *same class of inventive* concept and each compound must be searched and examined on its own, the restriction under 37 CFR 1.499 is proper.

In addition, the examiner has provided a reference anticipating the claims when R^5-R^6 forms a piperidine ring i.e. CA 105 which the International Search report failed to identify, thus, clearly indicated the tremendous burden resulting in incompleteness *without* restriction.

The requirement is still deemed proper and is therefore made FINAL.

Base on the election, the subject matter of claim 6 and 23 wherein R^5 and R^6 are independent substituents are examined. Claims 1-5, 9, 17-28 reading on the scope of Ar^1 is unsubstituted or substituted phenyl, Ar^2 is thienyl, R^5 and R^6 are independent substituents will be examined together with the election of claims 6 and 23 wherein R^5 and R^6 are independent substituents.

Claims 10-16 remained withdrawn being in nonstatutory "use" format because such claims provided for the use of compounds, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to

encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claims 10-16, were not withdrawn, would also be rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Further, such claims 10-16, were they not withdrawn, would be rejected under 35 USC 112 second and first paragraph because the scope of the terms "associated" is unclear. Associated with JNC pathway includes both inhibition and enhancement of the pathway for which descriptive support for a single compound being *"inhibiting and enhancing"* the pathway simultaneously is lacking and the limited description that the compounds can treat epilepsy, Huntington's disease, Parkinson's disease etc. employing a JNK inhibitory effective amount of the claimed compounds does not provide descriptive support and enablement to the claimed scope of using the compounds in all JNK associated pathway (see Medline PMID:12769633).

3. Claims 1-9, 17-28 are rejected under 35 U.S.C. 112, second paragraph, as failing to set forth the subject matter which applicants regard as their invention. It is very confusing as to "what" is the claimed invention and whether the compounds of claim 9 is the same invention as the base claim 1.

It is noted that on pages 7-8 of the specification wherein the scope of "substituted and unsubstitued" was defined, the substituent ***chlorine***/chloro- was **not** found i.e. would not be included in the base claim 1 for substituted Ar^1 or Ar^2 since descriptive support or antecedent basis for such substitution is lacking. However, all the compounds of claim 9 has 4-chloro – substitution on the phenyl ring. Therefore, the invention of claims 1-8, 17-28 and claim 9 are not identical. Therefore, claim 9 is improperly dependent on claim 1. Claim 1 lacks enabling support since the "substituted or unsubstituted" compounds of claims 1-8, 17-28 lacks the same utility as the exemplified compounds of claim 9.

It is further noted that on pages 10-11 the scope of amino acid residue was defined and in claim 1 the proviso "whereby at least one of R^3 and/or R^4 **must** be an amino acid residue".

Based on the description on pages 10-11, one of R^3 and/or R^4 **must** be a one valence moiety of amino acid such as the natural amino acid found in textbooks (see Wilbraham attached). As it can be seen from the textbook, a one valence amino acid moiety can be from the carboxyl end, from the amino end, from a side chain or the α-carbon (see Wilbraham particularly notation on page 222). Please note that ***none*** of the compounds of claim 9 has this amino acid residue structure at R^3 and/or R^4. Therefore, claim 9 is improperly dependent on claim 1. Claim 1 lacks enabling support since the "whereby at least one of R^3 and/or R^4 **must** be an amino acid residue" compounds of claims 1-8, 17-28 lacks the same utility as the exemplified compounds of claim 9.

Where applicant acts as his or her own lexicographer to specifically define a term of a claim contrary to its ordinary meaning, the written description must clearly redefine the claim term and set forth the uncommon definition so as to put one reasonably skilled in the art on notice that the applicant intended to so redefine that claim term. *Process Control Corp. v. HydReclaim Corp.*, 190 F.3d 1350, 1357, 52 USPQ2d 1029, 1033 (Fed. Cir. 1999). The term "natural amino acid residue" in claims 1-8, 17-28 is used by the claim to mean " alanyl, phenyalanyl, tyrosyl, vayl....etc", while the Wilbraham textbook evidenced that none of the exemplified compounds corresponding to such one valence moiety. The term is indefinite because the specification does not clearly redefine the term by structural bonding arrangement as to how they are bonded to the basic molecule and what is considered the "residue" portion of the amino acid in the claimed structure.

Claims 1-8, 17-28 are rejected under 35 USC 112 second paragraph for employing the format "comprising or consisting of...." which is improper Markush format, because Markush alternatives should employ the format of "consisting of..... and...". Applicants are urged to follow instruction of MPEP 2173.05(h) and make correction on all the claims.

4. Claims 1-4, 6-8, 17-21, 23-28 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, because the specification, while being enabling for naturally occurring amino acid, does not reasonably

provide enablement for the claimed scope of "natural amino acid or synthetic amino acid". The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The term "natural amino acid residues or synthetic amino acid residues" lacks descriptive and enabling support from the specification. It is noted that the chemical structure of the natural amino acid is conventionally known in the art and finds descriptive support in the specification. No description or enabling support can be found for "synthetic amino acid" or its residue. Please note that chemically, an amino acid is a compound with both an amino functional group and a carboxylic acid functional group including small molecules such as aminobenzoic acid (see RN 150-13-0) to polymeric compounds of US 3,396,030 (see col. 5 line 49) for which description and enabling support are lacking in the specification. In addition, without description, the meets and bounds of the term "synthetic amino acid residue" can not be ascertained and without description and provision of starting material, one having ordinary skill has not been given guidelines as to how such compounds or residues can be made.

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.
>
> (g)(1) during the course of an interference conducted under section 135 or section 291, another inventor involved therein establishes, to the extent permitted in section 104, that before such person's invention thereof the invention was made by such other inventor and not abandoned, suppressed, or concealed, or (2) before such person's invention thereof, the invention was made in this country by another inventor who had not abandoned, suppressed, or concealed it. In determining priority of invention under this subsection, there shall be considered not only the respective dates of conception and reduction to practice of the invention, but also the reasonable diligence of one who was first to conceive and last to reduce to practice, from a time prior to conception by the other.

Claims 1-8, 17-24, 26-28 are rejected under 35 U.S.C. 102(e) against the 371 date or 102(f) or (g) against the priority date as being anticipated by Thompson et al. US 6,503,901.

See compound at col. 55, example 42 (delineation of CAS structure at margin) anticipated the claims wherein Ar^1 is phenyl, X is O, R^1 is H, n=1, Ar^2 is thienyl, R^2 is H R^3 is the side chain residue of leucine, R^4 is H, R^5 is H, R^6 is substituted heteroaryl or substituted cyclic C_4-C_8-alkyl containing 2 heteroatoms fused with an aryl, and process of col. 45-46, for treating Alzheimer's disease (see col. 107-108).

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.
>
> (g)(1) during the course of an interference conducted under section 135 or section 291, another inventor involved therein establishes, to the extent permitted in section 104, that before such person's invention thereof the invention was made by such other inventor and not abandoned, suppressed, or concealed, or (2) before such person's invention thereof, the invention was made in this country by another inventor who had not abandoned, suppressed, or concealed it. In determining priority of invention under this subsection, there shall be considered not only the respective dates of conception and reduction to practice of the invention, but also the reasonable diligence of one who was first to conceive and last to reduce to practice, from a time prior to conception by the other.

Claims 1-8, 17-24, 26-28 are provisionally rejected under 35 U.S.C. 102(e) (f) or (g) as being anticipated by the US corresponding pending case of EP1,085,011.

The published EP 1,085,011 serves as evidence for the corresponding pending US 09/396,523 application since which is not issued yet.

See compound 1241 at fig. 456, page 98 first compound, which anticipated the claims wherein Ar^1 is phenyl, X is O, R^1 is H, n=1, Ar^2 is thienyl, R^2 is H R^3 is the side chain residue of leucine, R^4 is H, R^5 is H, R^6 is substituted alkyl, for treating immune system, tumor or angiogenesis etc. (p.43 claims).

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-8, 17-24, 26-28 are provisionally rejected under 35 U.S.C. 103(a) as being unpatentable over Vermeulin et al. US 6,172,261 in view of EP 1,085,011.

Determination of the scope and content of the prior art (MPEP §2141.01)

Vermeulin et al. '261 disclose antitumor structurally similar compounds of the claims and a species is noted at figure 2/5 compound 45, col. 8 lines 1-50.

Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

The difference of the exemplified compound 45 and the instant claims is that instead of branched chain at R3 and R4 structure, the prior art compound has a C5 straight chain. EP 1,085,011 in the same field of endeavor disclosed that the R3-R4 structure corresponding to the C5 straight chain is optionally branched with variation of position on the chain (see fig. 2/5 #45 vs fig 456 compound 1233 p.97,compound 1241 and 1340 p.98).

Finding of prima facie obviousness---rational and motivation (MPEP§2142-2143)

One having ordinary skill in the art would find the instant claims prima facie obvious **because** Vermeulin '261 explicitly taught structurally similar compounds and Vermeulin EP '011 taught the variation of this basic compound with modification of chain variation including the instant amino acid side chain i.e. compound 1241. One skilled in the art in possession of the two Vermeulin references would be in possession of the instantly claimed compounds for treating tumor etc. since the mechanism of treatment is immaterial the identical compounds are known for the targeted disease.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celia Chang whose telephone number is 703-308-4702. The examiner can normally be reached on Monday through Thursday from 8:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner can be reached by facsimile at (703) 308-7922 with courtesy voice message supra.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

Celia Chang
Primary Examiner
Art Unit 1625

OACS/Chang
June 26, 2003